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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,243	01/04/2002	**Paul I. Freimuth**	BSA 01-22	6646

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EXAMINER	
HIBBERT, CATHERINE S	
ART UNIT	**PAPER NUMBER**
1636	

NOTIFICATION DATE	DELIVERY MODE
07/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/037,243	FREIMUTH ET AL.	
	Examiner	Art Unit	
	CATHERINE HIBBERT	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64 and 101-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64 and 101-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants Amendment to the Claims, filed 14 April 2009, is received and entered for Application No. 10/037,243, filed 4 January 2002. Claims 1-63 and 65-100 are cancelled. Claims 101-103 are new. Claim 64 is currently amended. Claims 64 and 101-103 are pending and under examination in this action. Applicants statement that all claims are readable on the elected species, the vector encoding the T7B peptide extension (SEQ ID NO:6), on page 16 of REMARKS filed 14 April 2009 is acknowledged. It is noted that claims are being examined to the extent they read on the elected species of the T7B peptide extension (SEQ ID NO:6).

Response to Amendments/Arguments

The rejection of Claim 64 under 35 U.S.C. 112, second paragraph, is **withdrawn** based on the Amendment to the Claims filed 14 April 2009.

The rejection of Claim 64 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, as a new matter rejection, is **withdrawn** based on the Amendment to the Claims filed 14 April 2009.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 64 stands rejected and new Claims 101-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freimuth et al in "Coxsackievirus and Adenovirus Receptor Amino-Terminal Immunoglobulin V-Related Domain Binds Adenovirus type 2 and Fiber Knob from Adenovirus Type 12" (Journal of Virology, February, 1999, Vol. 73, No.2, pages 1392-1398; made of record in the IDS), in view of Condron et al in "Frameshifting in gene 10 of bacteriophage T7" (J Bacteriol 1991, Vol. 173 No. 21, pages 6998-7003; made of record in the IDS and as cited in the Score Report for SEQ ID NO:6, Result 1, of record).

Initially it is noted that the claims reads on a composition and as such the intended use language in the claims that pertain to the term "for enhancing the solubility

and proper folding of a protein or polypeptide of interest" (Claims 64 and 101-103) and regarding Claim 64, the term

> for inserting, in-frame with said first nucleic acid sequence, a second nucleic acid sequence encoding a protein or polypeptide of interest, said protein or polypeptide having a carboxyl- and an amino- terminus, wherein expression of the first and second nucleic acid sequences yields a fusion protein consisting of the encoded peptide extension fused to the carboxyl-terminus of the protein or polypeptide of interest, and wherein the protein or polypeptide of interest exhibits poor solubility and/or improper folding when expressed in the absence of fusion to said peptide extension,

does not bear patentable weight when applying prior art to the claims. Thus, the Claim 64, as written, can be interpreted to read on any pET-15b expression vector comprising a first nucleic acid sequence encoding a peptide extension, wherein the encoded peptide extension is Peptide T7B (SEQ ID NO: 6), the expression vector further comprising a multiple cloning site.

Freimuth et al teach a pET-15b expression vector comprising a multiple cloning site and a nucleic acid sequence encoding a peptide extension that increases the solubility of the linked fusion protein (e.g. page 1393, Figure 1(C) and legend; page 1394, ¶ bridging left and right column). Freimuth et al teach that the peptide extension contains the 22 amino acid sequence LEDP/AANKARKEAELAAATAEQ. It is noted that the peptide extension of Freimuth et al is the four amino acids LEDP contiguously in sequence with the carboxyl-terminal 18 residues of the phage T7 gene 10B protein.

Freimuth et al differ from the invention claimed in the instant Claim 64 because Freimuth et al fail to teach the peptide extension is the T710B (SEQ ID NO:6). It is noted that SEQ ID NO:6 is a 44 amino acid sequence that begins with the first four

amino acids of the peptide extension of Freimuth et al (LEDP) contiguously in sequence with the carboxyl-terminal 40 residues of the phage T7 gene 10B protein.

The Score Report, in light of Condron et al teach the amino acid sequence of the T7 gene 10B protein, including the carboxyl-terminal 40 residues.

Absent evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the 40 amino acid residue sequence for the 18 amino acid residue sequence of the phage T7 gene 10B protein (see Score Report of SEQ ID NO:6 and Cordon et al) in the pET15b vector containing the 22 peptide extension taught in Freimuth et al because Cordon et al (see SCORE report) teach the 40 amino acid sequence of the carboxyl-terminal 10B protein was known and Freimuth et al proposed using mutagenesis approaches, regarding the 22 amino acid peptide extension study, for the optimization of Ad2 knob solubility. (It is noted that Ad2 knob is a protein of interest tested in the expression vector containing the 22 amino acid peptide extension). Since the 22 amino acid extension consisted of the last 18 amino acids of the 10B gene, it would have been obvious to one of ordinary skill in the art for the "mutagenesis" regarding the solubility peptide extension to include addition of the next contiguous amino acids starting from the last 18 amino acids of the 10B gene, as shown in Applicants invention (page 1397, right column, paragraph 2).

One would have been motivated at the time the invention was made to have extended the peptide extension substituting the longer peptide extension containing the carboxyl-terminal 40 amino acid residues of the phageT7 gene 10B protein because Freimuth et al stated that the solubility of a D1 protein depended on the presence of the

22 amino acid peptide extension (page 1397, left column, paragraph 4) but that the solubility of a different protein of interest, the Ad2 protein, was not as effected by the same vector sequences and further stated that "optimization of Ad2 knob solubility through mutagenesis approaches could provide insights into intrinsic factors that regulate protein folding and multimerization in vivo (page 1397, right column, paragraph 2).

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because Freimuth et al showed that the substitution of various length peptide extensions into expression vectors was successfully practiced at the time Freimuth et al and Cordon et al were published.

In view of the foregoing, the vector of claims 64 and 101-103, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC *§103(a)*.

Applicants response is to traverse the rejection under 103(a). Initially, Applicants note that the named inventors contributed to each of the claims remaining in the application and submit that their inventive contributions were made prior to the initial date of filing of this invention, and can be traced to preceding the date of preparation of the initial draft of the application, and preceding the date of signing of the Record of Invention filed with the office at Brookhaven, i.e., prior to November 7, 2000.

Regarding the rejection of Claim 64 as unpatentable over Freimuth et al in view of Condron et al, Applicants traverse, stating:

> In the cited Freimuth et al article, a fortuitous cloning of the extracellular domains of the **c**oxsackie virus/**a**denovirus **r**eceptor (CAR) protein, including the D1and the combined D1/D2 domain, into pET-15b using the *Nco1-Xho1* restriction sites lead to the D1 domain (as well as the D1/D2 domain) being expressed as a fusion protein in which the vector-encoded peptide sequence LEDPAANKARKEAELAAATAEQ (peptide T7A, SEQ ID NO:20 of the present application) was fused at the carboxyl terminus of the D1 domain. The resultant expressed D1 fusion protein was found to be more soluble (but only at 18°C) than the D1 domain expressed without the 22 amino acid extension (i.e., when cloned in pET20b or when cloned in pET 15b with a stop codon inserted in such a way as to eliminate fusion with the 22 amino acid extension) (see, in Freimuth et al the paragraphs of the section entitled "Expression and purification of CAR extracellular fragments", pages 1393-1394).

In addition, Applicants argue that

> Condron et al teach that the product of gene 10 of bacteriophage T7 (i.e., the phage gene 10 protein) is expressed in two forms, the normal, 10A form and an extended, 10B form as a result of a frameshift occurring during translation. the 10B protein contains 52 extra amino acids at the carboxyl terminus compared to the 10A protein. Condron et al, and particularly Dunnand Studier (J.Mol. Biol. (1983) 166:477-535), teach that the 10B protein is formed as a result of a frameshift during translation and the aberrant 10B protein then becomes a minor component of the T7 phage capsid. The amino acid sequence encompassing the 52 amino acid extension (Condron et al) was originally implied from the known sequence of the phage T7 DNA . The -1 frameshift leading to the 10B protein was first taught in Dunn and Studier, J. Mol. bio. (1983).

Thus, Applicants representative submits that

> Freimuth et al could not have taught (and therefore "fail to teach") "the peptide extension is the T710B (SEQ ID NO:6) (sic)". The peptide extension of Freimuth et al is not the T710B peptide (SEQ ID NO:6) and is not a 44 amino acid sequence but is T&A, a 22 amino acid sequence, noted SEQ ID NO:2 in the present specification. Applicants representative further points out that the reference SEQ IDN NO:6 is named peptide extension T&B and not T&10B. Applicants Agent notes that there may be "some confusion in an unfortunate overlap in nomenclature between the phage 10B protein and the peptide extension designated as T7B (seq ID no:6) and perhaps the peptide extension T7B10 (SEQ ID NO:16)".

Furthermore, Applicants representative argues that

> First, while agreeing that Condron et al (and particularly through work of Dunn and Studier, J. Mol. Biol. (1983)) teach the extension of the phage 10A protein to form the 10B protein, Applicants representative rebuts the obviousness of the choice of the carboxyl terminal 40 amino acids of the phage T7 10B protein to form peptide extension T7B (SEQ ID NO:6). If this had been an obvious choice, why wasn't it obvious to choose the last 35 amino acids, or the last 28 or the last 48? The list of choices as to what to "substitute for the 18 residue sequence" is extensive - and could have been peptides increasing monotonically in length with each additional amino acid starting with the 18 of Freimuth et al. and extending to the complete phage T7 10B protein 52 amino acid extension (i.e., to the claimed T7C peptide extension (SEQ ID NO:5)). Instead the invention claimed (in addition to peptide T7C) is the 40 amino acid sequence and amino acid variants thereof as well as amino acid variants of the original 18 amino acids taught by Freimuth et al.

In addition, Applicants representative argues that

> with respect to the remarks suggesting that Freimuth et al proposed using "mutagenesis approaches, regarding the 22 amino acid peptide extension study, for optimization of Ad2 knob solubility", the representative for the Applicants respectfully submits that the Examiner has misrepresented the proposed uses of mutagenesis in the teachings of Freimuth et al. (As an aside, the representative further notes that the peptide extension was not used in conjunction with expression of any of the adenovirus knob proteins in Freimuth et al or in the work cited in Freimuth et al.) Freimuth et al propose using mutagenesis for two very different purposes than the one suggested in the Examiner's remarks.

Applicants representative continues that

> In Freimuth et al, the word mutagenesis appears twice. First, in the left column of page 1397, wherein Freimuth et al suggest using mutagenesis approaches to examine which amino acids of the CAR protein and of the adenovirus knob

protein are important in generating the specific interaction between these two protein entities: "The importance of these amino acids to knob-CAR binding could readily be tested through site-directed mutagenesis of the recombinant proteins we describe here." This most assuredly has nothing to do with modifying the peptide extension of Freimuth et al to form the peptide extensions of the invention under examination. The second recitation of "mutagenesis" in Freimuth et al appears in the penultimate paragraph of the article in the right column of page 1397: "Optimization of Ad2 knob solubility through mutagenesis approaches could provide insights into intrinsic factors that regulate protein folding and multimerization in vivo." This follows a discussion of the differences in the yields and solubility of the recombinant knob proteins from two different adenovirus serovars, Adl2 and Ad5 using bacterial expression systems. This discussion concludes: "... therefore, the differences in yields of the soluble knob proteins must reflect differences in knob folding and trimerization in bacterial cells." This suggested use of mutagenesis has nothing at all to due with amino acid substitutions of the peptide extension of Freimuth et al nor the variants presently claimed. The Agent submits that neither of the proposed uses of mutagenesis relate at all to substituting the 18 amino acid extension with a longer extension. Furthermore, and perhaps more importantly, neither of the proposed uses of mutagenesis in Freimuth et al would include changing the T7 phage gene 10B sequence (as is done in the present invention) to create peptide extensions having altered amino acids that further enhance the solubility-enhancing properties of the peptide extensions and which variant peptide extensions are claimed in the present invention.

Furthermore, Applicants representative first points out the above discussion on the proposed mutagenesis studies of Freimuth et al and secondly points to “the parenthetic remark on page 11 of this paper”, arguing that “none of the adenovirus knob proteins discussed in Freimuth et al. were expressed with a peptide extension”. Thus, Applicants

representative argues that “it would have been impossible to determine” whether or not, the Ad2 protein was not as effected by the same vector sequences. Thirdly, Applicants representative points out that “the neither Condron et al nor the work of Dunn and Studier (1983) suggest that the T7 10B protein is or is not more soluble than the shorter, normal T7 10A protein. If they had made some suggestion of that nature one may have been motivated to substitute the entire gene 10B extension for the 22 amino acid extension. However this teaching as motivation is absent”. In addition Applicants representative argues that “although Freimuth et al state that the solubility of a D1 protein depended the presence of the 22 amino acid extension on page 1397, on page 1394, right column, at the end of the first partial paragraph they also state, perhaps more accurately, that "... these data indicate that D1 solubility in *E. coli* ceils is enhanced by the pET15b-encoded 22-amino acid carboxy-terminal extension". This is because D1 was only soluble when expressed as a fusion if expression was carried out at 18°C. This is further supported in the specification- see page 29, lines 1 through 6.

In addition, Applicants representative argues that

> it is unclear that one of skill in the art would be motivated to substitute a longer peptide extension merely because the 22 amino acid peptide extension enhanced the solubility of the D 1 domain of the CAR protein. There is little motivation supplied in the cited references either singly or in combination. This is particularly evidenced in the present specification in which it was clearly demonstrated that 22 amino acid peptide extensions having amino acid substitutions of the 22 amino acid peptide extension of Freimuth et al served to better enhance the solubility of D1 without resorting to the use of a longer sequence (see lines 1 through 7, page 34 of the specification).

In addition, Applicants representative argues the suggestion of a

reasonable expectation of Success, stating that:

> The Agent and the Applicants fully agree that Condron et al teach (especially in combination with Dunn and Studier (1983)) the carboxyl-tenm'na140 residues of the T7 gene 10B protein. However, the Agent for the Applicants respectfully submits that the fortuitous cloning and resultant enhancement of Solubility of the CAR D 1 protein through extension with the 22 amino acids in Freimuth et al would NOT obviously or otherwise lead one to predict or assume one would achieve success by substituting a longer peptide extension. This is further supported by noting that Condron et al and Dunn and Studier make no suggestions or teachings that the phage T7 10B protein is or is not "more soluble" than the 10A protein. Thus, the revelation of the sequence of the T7 gene 10B as an extension of the T7 gene 10A protein ofT7 phage capsids in Condron et al and the 22 amino acid extension of Freimuth et al would not lead one to suggest or imply or expect success with a 44 (40 amino acids from gene 10B protein plus LEDP) amino acid extension. Again, as above, if merely lengthening the extension was better, why not extend the 22 amino acid peptide to 35 amino acids, or 28 or 48?
>
> Further, if it was a general phenomenon that the "gene 10B type" extensions were appropriate for enhancing solubility and proper folding of recombinant proteins, one might expect that the phage T3 10B extension would be appropriate as well. As one can see in the present specification, the T3 gene 10B extension did not enhance solubility (page 28, line 10 through page 29, line 6).

In addition, Applicants representative argues that

> The Examiner's comment: "Freimuth et al showed that the substitution of various length peptide extensions into expression vectors was successfully practiced at the time Freimuth et al and Cordon *(sic)* et al were published", is confusing such that the representative for the Applicants cannot determine whether the Examiner is referring to the present specification showing that various length peptide extensions was successfully practiced or whether Freimuth et al showed use of various length peptide extensions. It is clear that the only "various length peptide extensions" that are taught are those of the present invention and that they were not taught in Freimuth et al.

Thus, Applicants representative concludes that "because of this confusion and in light of

the above rebuttal of the obviousness rejection, the representative requests the

Examiner's consideration of the above remarks as being persuasive that the invention

being examined could not have been obvious under the combination of the cited references".

Applicants response has been fully considered but is respectfully not found persuasive for reasons of record and because it is noted that SEQ ID NO:6 is a 44 amino acid sequence that begins with the first four amino acids of the peptide extension of Freimuth et al (LEDP) contiguously in sequence with the carboxyl-terminal 40 residues of the phage T7 gene 10B protein. The Score Report, in light of Condron et al teach the amino acid sequence of the T7 gene 10B protein, including the carboxyl-terminal 40 residues.

Absent evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the 40 amino acid residue sequence for the 18 amino acid residue sequence of the phage T7 gene 10B protein (see Score Report of SEQ ID NO:6 and Cordon et al) in the pET15b vector containing the 22 peptide extension taught in Freimuth et al because Cordon et al (see SCORE report) teach the 40 amino acid sequence of the carboxyl-terminal 10B protein was known and Freimuth et al proposed using mutagenesis approaches, regarding the 22 amino acid peptide extension study, for the optimization of Ad2 knob solubility. (It is noted that Ad2 knob is a protein of interest tested in the expression vector containing the 22 amino acid peptide extension). Since the 22 amino acid extension consisted of the last 18 amino acids of the 10B gene, it would have been obvious to one of ordinary skill in the art for the "mutagenesis" regarding the solubility peptide extension to include

addition of the next contiguous amino acids starting from the last 18 amino acids of the 10B gene, as shown in Applicants invention (page 1397, right column, paragraph 2).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Freimuth et al teach a pET-15b expression vector comprising a multiple cloning site and a nucleic acid sequence encoding a peptide extension that increases the solubility of the linked fusion protein (e.g. page 1393, Figure 1(C) and legend; page 1394, ¶ bridging left and right column). Freimuth et al teach that the peptide extension contains the 22 amino acid sequence LEDP/AANKARKEAELAAATAEQ. It is noted that the peptide extension of Freimuth et al is the four amino acids LEDP contiguously in sequence with the carboxyl-terminal 18 residues of the phage T7 gene 10B protein. Cordon et al (see SCORE report) teach the 40 amino acid sequence of the carboxyl-terminal 10B protein was known and Freimuth et al proposed using mutagenesis approaches, regarding the 22 amino acid peptide extension study, for the optimization of Ad2 knob solubility. (It is noted that Ad2 knob is a protein of interest tested in the expression vector containing the 22 amino acid peptide extension). Since the 22 amino acid extension consisted of the last 18 amino acids of the 10B gene, it would have been obvious to one of ordinary

skill in the art for the "mutagenesis" regarding the solubility peptide extension to include addition of the next contiguous amino acids starting from the last 18 amino acids of the 10B gene, as shown in Applicants invention (page 1397, right column, paragraph 2).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Regarding the arguments against motivation, one would have been motivated at the time the invention was made to have extended the peptide extension substituting the longer peptide extension containing the carboxyl-terminal 40 amino acid residues of the phageT7 gene 10B protein because Freimuth et al stated that the solubility of a D1 protein depended on the presence of the 22 amino acid peptide extension (page 1397, left column, paragraph 4) but that the solubility of a different protein of interest, the Ad2 protein, was not as effected by the same vector sequences and further stated that "optimization of Ad2 knob solubility through mutagenesis approaches could provide insights into intrinsic factors that regulate protein folding and multimerization in vivo (page 1397, right column, paragraph 2).

Therefore, Claim 64 stands rejected and new Claims 101-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freimuth et al, in view of Condron et al in and as cited in the Score Report for SEQ ID NO:6, Result 1).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE HIBBERT, whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,

Catherine S. Hibbert
Examiner/AU1636

/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1636